TUBERCULOSIS

DISEASE REPORTING

In Washington

DOH receives approximately 250 to 300 reports of tuberculosis (TB) per year, for an average rate of 4.8/100,000 persons. An average of 4 deaths are reported to be associated with tuberculosis each year.

Purpose of reporting and surveillance

- To identify and ensure the adequate evaluation and treatment of persons with TB.
- To identify the contacts of TB cases and ensure their evaluation.
- To ensure that all eligible infected contacts are offered and complete preventive therapy.

Reporting requirements

- Health care providers: **immediately notifiable**
- Hospitals: **immediately notifiable**
- Laboratories: **notifiable within 2 workdays** to DOH-TB Services (206-361-2838); antibiotic sensitivity testing (first isolates only); specimen submission required
- Local health jurisdictions: **notifiable within 7 days** of case investigation completion or summary information required within 21 days

CASE DEFINITION FOR SURVEILLANCE

Suspect case

Any person who reports clinical symptoms associated with TB (e.g., productive, prolonged cough, chest pain, hemoptysis, fever, chills, loss of appetite, or weight loss) and is evaluated by a medical practitioner for tuberculosis, which may include diagnostic x-rays and bacteriology collection, is considered a suspect. All practicing physicians are required by Washington State law to report all suspects of TB to their local health authorities within 24 hours of evaluation (WAC 246.100.076); in turn, local health authorities are required to report these suspects within seven days to the state TB Control Program (WAC 246.100.091b).

Confirmed case

The Centers for Disease Control and Prevention (CDC) has outlined two sets of case-defining criteria, laboratory confirmed and clinically confirmed. A person suspected of having TB must meet one of the two following case definitions to be considered an active case.

Case definition

Laboratory Case Definition
(*must meet ANY of the following criteria*)

- Isolation of *Mycobacterium tuberculosis* using culture techniques from a clinical specimen; or
- Demonstration of *Mycobacterium tuberculosis* from a clinical specimen by DNA probe or mycolic acid pattern on high-pressure liquid chromatography; or
- Demonstration of acid-fast bacilli in clinical specimen when a culture has not been or cannot be obtained in a patient with clinical symptoms of tuberculosis.

Clinical Case Definition
(*must meet ALL of the following criteria*)

- Positive tuberculin skin test (negative test is allowed for those patients with proven anergy or an AIDS diagnosis); and
- Other signs and symptoms compatible with TB, such as an abnormal or unstable chest x-ray or clinical evidence of current disease; and
- X-ray improvement on chemotherapy; and
- Treatment with two or more anti-tuberculosis medications; and
- Completed diagnostic evaluation.

A. DESCRIPTION

1. Identification

Tuberculosis is a mycobacterial disease that is important as a major cause of disability and death in many parts of the world. The initial infection usually goes unnoticed; tuberculin skin test sensitivity appears within 2-10 weeks. Early lung lesions commonly heal, and leave no residual changes except occasional pulmonary or tracheobronchial lymph node calcifications. Approximately 90%-95% of those initially infected enter this latent phase from which there is a lifelong risk of reactivation. Appropriate completion of preventive chemotherapy can reduce the lifetime risk of clinical tuberculosis (TB disease) by 95% and is still effective in persons with HIV infection. Approximately 5% of apparently normal hosts and as many as 50% of persons with advanced HIV infection may progress directly to pulmonary tuberculosis or, by lymphohematogenous dissemination of bacilli, to pulmonary, miliary, meningeal or other extrapulmonary involvement. Serious outcome of the initial infection is more frequent in infants, young adults and the immunosuppressed.

Extrapulmonary TB occurs less commonly than pulmonary TB. Children and persons with immunodeficiencies such as from HIV infection have a higher proportion of extrapulmonary TB, but pulmonary disease remains the most common type of TB disease worldwide, even in these more susceptible groups. TB disease may affect any organ or tissue such as the lymph nodes, pleura, pericardium, kidneys, bones and joints, larynx, middle ear, skin, intestines, peritoneum and eyes.

Progressive pulmonary TB arises from exogenous reinfection or endogenous reactivation of a latent focus remaining from the initial infection. If untreated, about half the patients will die within 5 years, a majority of these within 18 months. Clinical status is based mainly on the presence or absence of tubercle bacilli in the sputum and changes seen on chest radiographs. Abnormal radiographic densities indicative of pulmonary infiltration, cavitation and fibrosis can occur before clinical manifestations. Fatigue, fever, night sweats and weight loss may occur early, while localizing symptoms of cough, chest pain, hemoptysis and hoarseness become prominent in advanced stages.

Immunocompetent people who are or have been infected with *Mycobacterium tuberculosis*, *M. africanum* or *M. bovis* will usually react to an intermediate strength tuberculin skin test, i.e., bioequivalent to 5 IUs of the International Standard of Purified Protein Derivative-Standard (PPD-S). A positive reaction is defined as either 5, 10, or 15 mm in duration based on the risk of exposure or disease. Ten to 20% of persons with active TB disease may not have any reaction to PPD. Therefore**, a negative skin test does not rule out active TB disease**. Induration of more than 5 mm is considered positive for household and/or close contacts of infectious TB disease cases, persons with an abnormal chest radiograph suggesting old healed TB disease, and persons with HIV infection. A diameter of 10 mm is considered positive for persons with medical risk factors (including diabetes mellitus, alcoholism and drug abuse), persons from high prevalence areas for tuberculosis, from areas of low socioeconomic status, residents and staff of long term care facilities (including jails and prisons), and children younger than 4 years of age.

A PPD of 15 mm or greater in diameter is considered positive for adults and children (4 years of age or older) who have no risk factors and who live in areas with few cases of tuberculosis.

Cutaneous skin tests for anergy are no longer recommended, even for high risk patients such as those with HIV infection. Routine skin testing of all children is no longer recommended in the USA. Children who should be tested immediately include those who are suspected of having active TB disease, those exposed to an active case, those immigrating from an endemic country, or those who have recently traveled to an endemic country and had close contact to local persons from those countries. Incarcerated individuals and persons with HIV infection or children residing in a household with an HIV infected person should be tested annually. Children should be tested every 2-3 years if they are exposed to persons at high risk of disease. Testing at 4-6 and 11-12 years of age is indicated if their parents immigrated from a high risk area or if the children reside in high risk communities.

In some persons with TB infection, delayed type hypersensitivity to tuberculin may wane with time. When these individuals are skin tested many years after their initial infection, they may have a negative reaction. However, the skin test may stimulate (i.e., boost) their ability to react to tuberculin and cause a positive reaction to subsequent tests. This “boosted” reaction may be mistaken as new infection. Boosting has also been reported in persons who have received BCG vaccine. If the reaction to the first test is classified as negative, a second test should be performed 1-3 weeks later. A positive reaction to the

second test probably represents a boosted reaction. On the basis of the second test result, the person should be classified as previously infected and managed accordingly. This would not be considered a skin test conversion. If the second test result is also negative, the person should be classified as uninfected. Two step testing should be used for the initial skin testing of adults who will be retested periodically, such as healthcare workers. Washington State has not advised two-step testing for refugees, elderly, or tuberculosis contacts. A presumptive diagnosis of active TB disease is made by demonstration of acid-fast bacilli in stained smears from sputum or other body fluids; a positive sputum smear justifies initiation of antituberculosis therapy. The diagnosis is confirmed, where resources permit, by isolation of organisms of the *Mycobacterium tuberculosis* complex on culture; this also permits determination of the drug susceptibility of the infecting organism. In the absence of bacteriologic confirmation, active disease can be presumed if there is strong clinical evidence of an ongoing disease process by histologic or radiologic studies in a patient with a positive tuberculin skin test.

2. Infectious Agent

Mycobacterium tuberculosis complex. This complex includes *M. tuberculosis* and *M. africanum* primarily from humans, and *M. bovis* primarily from cattle. Other mycobacteria occasionally produce disease clinically indistinguishable from tuberculosis; the etiologic agents can be identified only by culture of the organisms. Genetic sequence analyses using PCR offers the potential for nonculture identification.

3. Worldwide Occurrence

Worldwide; industrialized countries had shown downward trends of mortality and morbidity for many years, but in the late 1980s reported cases reached a plateau and then increased in areas and population groups with a high prevalence of HIV infection or with large numbers of persons from areas with a high prevalence of tuberculosis. Mortality and morbidity rates increase with age, and in older people rates are higher in males than in females. TB morbidity rates are much higher among the poor, and usually higher in cities than in rural areas.

In the USA, the incidence of TB disease has declined since 1994, when the reported incidence of TB disease was 9.4/100,000 population (over 24,000 verified cases). In low incidence areas, including many areas in the USA, most TB disease in adults results from reactivation of latent foci that remain from an initial TB infection. In some large urban areas about 1/3 of TB disease cases resulted from recent infection. Although TB disease ranks low among communicable diseases in infectiousness per unit time of exposure, the long exposure of some contacts, notably household associates, may lead to a 30% risk of becoming infected. For infected children, the lifetime risk of developing disease may approach 50%. For people coinfected with HIV, the annual risk has been estimated at 2%-7% and the cumulative risk at about 60-80%. Epidemics have been reported among people congregated in enclosed spaces, such as nursing homes, shelters for the homeless, hospitals, schools, prisons and office buildings. From 1989 to the early 1990s, extensive propagated outbreaks of multidrug resistant TB, defined as resistant to at least isoniazid

and rifampin, have been recognized in settings where many HIV infected persons are congregated (hospitals, correctional facilities, drug treatment clinics and HIV residences). These outbreaks have been associated with high mortality rates and with transmission of *M. tuberculosis* to health care workers. Strict enforcement of infection control guidelines have been effective in combating and preventing these outbreaks.

The prevalence of TB infection detected by tuberculin testing increases with age. The incidence of infection in developed countries has declined rapidly in recent decades; in the USA, the annual risk of new infection is estimated to average about 10/100,000 people or less, although there probably are areas in the USA with a relatively high annual risk of new infection. In areas where human infection with mycobacteria other than tubercle bacilli is prevalent, cross reactions complicate interpretation of the tuberculin reaction.

Infection with *M. bovis*, the bovine tubercle bacillus, in humans is rare in the USA, but is still a problem in some areas, such as the border with Mexico, where the disease in cattle has not been controlled and milk and milk products are consumed raw.

4. Reservoir

Primarily humans, rarely primates; in some areas, diseased cattle, badgers, swine, and other mammals are infected.

5. Mode of Transmission

Exposure to tubercle bacilli in airborne droplet nuclei produced by people with pulmonary or laryngeal tuberculosis during expiratory efforts, such as coughing, singing or sneezing. Health care workers are exposed during medical procedures such as bronchoscopy, autopsy and intubation. Laryngeal tuberculosis is highly contagious. Prolonged close exposure to an infectious case may lead to infection of contacts. Direct invasion through mucous membranes or breaks in the skin may occur but is extremely rare. Bovine tuberculosis results from exposure to tuberculous cattle, usually by ingestion of unpasteurized milk or dairy products, and sometimes by airborne spread to farmers and animal handlers. Except for rare situations where there is a draining sinus, extrapulmonary tuberculosis (other than laryngeal) is generally not communicable.

6. Incubation period

From infection to demonstrable primary lesion or significant tuberculin reaction, about 2-10 weeks. While the subsequent risk of progressive pulmonary or extrapulmonary TB is greatest within the first year or two after infection, latent infection may persist for a lifetime. HIV infection appears to increase the risk greatly and shorten the interval for the development of TB disease.

7. Period of communicability

Theoretically, as long as viable tubercle bacilli are being discharged in the sputum. Some untreated or inadequately treated patients may be sputum positive intermittently for years. The degree of communicability depends on the number of bacilli discharged, the virulence of the bacilli, adequacy of ventilation, exposure of the bacilli to sun or UV light, and opportunities for their aerosolization by coughing, sneezing, talking or singing, or during high risk medical procedures such as autopsies, intubations or bronchoscopies. Effective antimicrobial chemotherapy usually eliminates communicability within a few weeks, at least in the household setting. Children with tuberculosis are generally not infectious.

8. Susceptibility and resistance

The risk of infection with the tubercle bacillus is directly related to the degree of exposure and does not appear to be related to genetic or other host factors. The most hazardous period for development of clinical disease is the first 6-12 months after infection. The risk of developing disease is highest in children under 5 years old, lowest in later childhood, and high again among adolescents, young adults, the very old and the immunosuppressed. Reactivation of long latent infections accounts for a large proportion of TB disease cases in older people. For infected persons, susceptibility to TB disease is markedly increased by HIV infection and other forms of immunosuppression, those underweight or undernourished, those with a debilitating disease such as chronic renal failure, cancer, silicosis, diabetes or postgastrectomy, or those who are substance abusers.

For adults with latent TB infection who are also infected with HIV, the lifetime risk of developing TB disease rises from an estimated 10% to 60-80%. This interaction has resulted in a parallel pandemic of TB disease: in some urban sub-Saharan African populations where 10-15% of the adult population have HIV and TB infections, annual TB disease rates have increased from 5-10 fold during the latter half of the 1990s.

B. METHODS OF CONTROL

1. Preventive measures:

a. Promptly identify, diagnose and treat potentially infectious patients with TB disease. Establish case finding and treatment facilities for infectious cases to reduce transmission.
b. Make available medical, laboratory and x-ray facilities for prompt examination of patients, contacts and suspects; facilities for early treatment of cases and people at high risk of infection; and beds for those needing hospitalization.

   In high incidence areas, examination of sputum by direct microscopy (by culture when possible) of those presenting at health facilities because of chest symptoms may give a high yield of infectious tuberculosis. In many situations, direct microscopy may be the most cost effective method of case finding and is the first

priority in developing countries. Because of recent outbreaks of multidrug resistant tuberculosis, all initial isolates in the USA should be submitted for drug susceptibility testing. In countries with limited resources or laboratory capacity, drug susceptibility testing may be limited to treatment failures and former defaulters.

c. Educate the public in mode of spread and methods of control and the importance of early diagnosis.
d. Reduce or eliminate those social conditions that increase the risk of infection, such as overcrowding.
e. TB prevention and control programs should be established in all institutional settings in which health care is provided and/or immunocompromised patients such as HIV infected persons may be congregated (e.g., hospitals, drug treatment programs, correctional facilities and homeless shelters).
f. Use preventive treatment with isoniazid, which has been shown to be effective in preventing the progression of latent TB infection to TB disease in a high proportion of individuals. Studies in adults with HIV infection have demonstrated the effectiveness of alternative regimens including shorter courses of rifampin and pyrazinamide. Preventive therapy is routinely indicated for infected persons, regardless of age. It is important to rule out active TB disease before starting preventive therapy, especially in immunocompromised persons such as HIV infected individuals.

   Persons started on preventive treatment should be informed of possible adverse effects, such as hepatitis, drug fever or severe rash, and advised to discontinue treatment and seek medical advice if any suggestive symptoms develop. Most health care providers obtain baseline liver function tests on all patients; it is especially important in older patients and those who abuse alcohol. Directly observed, supervised preventive therapy (DOPT) should be used. (e.g., in correctional facilities, some drug treatment programs, schools). No more than one month's supply of medication should be given at any time. Patients should be queried at least monthly about adverse effects. Biochemical monitoring for hepatitis need not be done routinely, but is mandatory if symptoms or signs of hepatitis occur.

   Isoniazid preventive therapy is contraindicated where there is a history of a previous severe adverse reaction to the drug or when there is acute liver disease of any etiology. During pregnancy, it may be wise to postpone preventive treatment until after delivery except in high risk individuals, and then it should be administered with caution. Isoniazid should be given with added caution to people who use alcohol regularly and those with chronic liver disease. Persons with hepatitis C infection may be at increased risk of isoniazid toxicity.

   A policy of preventive treatment is unrealistic and unsuitable for mass application in most community health programs unless there is a well-organized program to supervise and encourage adherence to therapy and the treatment program for patients with active TB disease can achieve a high rate of cure. Persons with HIV infection and a positive PPD who do not have active TB disease should receive preventive therapy.
g. Provide public health nursing and outreach services for direct supervision of patient therapy, and arrange for the examination and preventive treatment of contacts.

h. Persons infected with HIV should be skin tested by the Mantoux method, using intermediate strength PPD at the time their HIV infection is identified and started on prophylactic treatment if they are PPD positive (5 mm or more of induration) and active TB disease has been ruled out. Conversely, all people with evidence of TB disease or TB infection should be considered for counseling and tested for HIV infection if appropriate counseling is available.
i. Persons with recent diagnosis of tuberculosis should receive an HIV test as duration of therapy is modified.
j. In the US and other industrialized areas where BCG immunization is not routinely carried out, groups at high risk of TB infection and/or HIV infection may be selectively tuberculin tested as a case finding measure, e.g., health care workers, foreign born persons from areas where tuberculosis is highly prevalent and groups at high risk for HIV infection such as prison inmates and injecting drug users. In population groups where disease still occurs, systematic tuberculin test surveys may be used to monitor trends in the incidence of infection. X-ray examination is especially indicated whenever persistent chest symptoms are noted and bacteriologic tests are negative. Prior BCG immunization may complicate the interpretation of a positive skin test in a child or a recently immunized adult. However, skin test reactions from BCG wane over time and strongly positive reactions or significant increases in reactivity in such individuals should be considered indicative of TB infection.
k. BCG immunization of uninfected (tuberculin negative) people can induce tuberculin reactivity in more than 90% of vaccinees. The protection conferred has varied markedly in different field trials, and is perhaps related to some special characteristics of the population, the quality of the vaccine, or the strain of BCG employed. Some controlled trials have provided evidence that protection may persist for as long as 20 years in high incidence situations, while others have shown no protection at all.

   Case-control and contact studies have consistently demonstrated protection against TB meningitis and disseminated disease in children less than 5 years old. Because the risk of infection is very low in the USA, BCG is not routinely used. BCG is not available in Washington State. BCG should be considered only for children with a negative PPD skin test who cannot be placed on preventive therapy but have continuous exposure to people with untreated or ineffectively treated active disease, or who have continuous exposure to patients infected by organisms resistant to isoniazid and rifampin and the child cannot be removed from the exposure. BCG is contraindicated for people with immunodeficiency diseases including HIV infection. WHO has permitted the administration of BCG to asymptomatic HIV infected children and those at high risk of acquiring HIV infection.
l. Eliminate bovine tuberculosis among dairy cattle by tuberculin testing and slaughter of reactors; pasteurize or boil milk.
m. Take measures to prevent silicosis among those working in industrial plants and mines.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority when diagnosis is suspected. Case report should indicate if it is bacteriologically positive or based on positive tuberculin reaction and clinical and/or x-ray findings. Health departments should maintain a current register of cases requiring treatment and be actively involved with planning and monitoring the course of therapy.
b. Isolation: For pulmonary tuberculosis, control of infectivity is best achieved by prompt specific four drug therapy, which usually produces sputum conversion within 4-8 weeks. Hospital treatment is necessary only for patients with severe illness and for those whose medical or social circumstances make treatment at home impossible. Adult patients with sputum positive pulmonary tuberculosis need to be placed in a private room with negative pressure ventilation. Patients should be taught to cover both mouth and nose when coughing or sneezing. Persons entering the room should wear personal respiratory protective devices capable of filtering submicron particles. Isolation is unnecessary for patients whose sputum is bacteriologically negative, who do not cough and who are known to be on adequate chemotherapy (based on known or probable drug susceptibility and a clear clinical response to therapy). Children with active TB disease and no cough and negative sputum smears are not contagious and do not require isolation. Adolescents should be managed as adults. The need to adhere to the prescribed chemotherapeutic regimen must be reemphasized repeatedly to all patients. Directly observed therapy should be used when logistically and financially feasible and in particular for persons with suspected drug resistance, a previous history of poor compliance to therapy, or who live in conditions in which relapse would result in exposure of many other persons.
c. Concurrent disinfection: Handwashing and good housekeeping practices should be maintained according to routine policy. There are no special precautions necessary for handling fomites (dishes, laundry, bedding, clothes and personal effects). Decontamination of air may be achieved by ventilation; this may be supplemented by ultraviolet light.
d. Quarantine: None.
e. Management of contacts: In the USA, preventive treatment for 3 months is recommended (see B1f, above) for skin test negative close contacts; the skin test should then be repeated to determine the need for additional preventive therapy. If repeat skin testing at 3 months is negative, therapy may be stopped. BCG immunization of tuberculin negative household contacts may be warranted under special circumstances (see above).
f. Investigation of contacts and source of infection: PPD testing of all members of the household and other close contacts is recommended in the USA. All contact investigations should be timely (within 2 weeks) ,accurate, and sensitive to the presence of the most vulnerable population- Children. If negative, a repeat skin test should be performed 2-3 months after exposure has ended. Chest radiographs should be obtained on positive reactors when they are identified. Preventive treatment is indicated (see B1f, above) for contacts who are positive reactors and for some initially negative reactors at high risk of developing active disease, especially

young (5 years old or younger) and HIV infected close contacts, at least until the repeat skin test is shown to remain negative. Unfortunately, in many developing countries, investigation of household contacts is limited to sputum microscopy of those contacts who have symptoms suggestive of TB disease.

g. Specific treatment: Directly observed therapy has been shown to be highly effective and is recommended for treatment of TB disease in the USA. Patients with TB disease should be given prompt treatment with an appropriate combination of antimicrobial drugs, with regular monitoring of sputum smears. For drug susceptible disease, a 6 month regimen consisting of isoniazid (INH), rifampin (RIF), and pyrazinamide (PZA) is recommended for the first 2 months followed by INH and PZA for 4 months. A 4 drug initial therapy (including ethambutol (EMB) or streptomycin (SM)) is recommended if the infection was acquired in areas where an increased prevalence of INH resistance has been reported. After drug susceptibility results are available, a specific drug regimen can be selected.

   If sputum fails to become negative after 2-3 months of regular therapy or reverts to positive after a series of negatives, or if clinical response is poor, examination for medication compliance and for bacterial drug resistance is indicated. Treatment failure is usually the result of irregularity in taking drugs and may not necessitate a change in regimen; a change in supervision may well be required if a favorable clinical response is not observed. At least two drugs to which the organisms are susceptible should be included in the regimen; a single new drug should never be added to a failing regimen. If INH or RIF cannot be included in the regimen, the minimum duration of therapy is 18 months after cultures have become negative.

   Children are treated with the same regimens as adults with some modifications. In children, susceptibility of the causative organism can often be inferred from testing isolates of the adult source case. Therapy for children with meningitis, miliary disease, or bone/joint disease should last for at least 9-12 months. Streptomycin is contraindicated during pregnancy.

   All drugs occasionally cause adverse reactions. Surgery is occasionally indicated, usually in multidrug resistant cases.

3. Epidemic measures

Alertness to recognize and treat aggregations of new infections resulting from contact with an unrecognized infectious case, and intensive search for and treatment of the source of infection.

4. International measures

Chest radiograph screening, PPD testing, and smear and culture testing of symptomatic PPD positive persons from high prevalence countries is suggested on immigration. WHO Collaborating Centres.